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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,656	10/24/2003	Igor Dozmorov	OMRF:013US	9649

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EXAMINER

MILLER, MARINA I

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/693,656

Applicant(s)

DOZMOROV ET AL.

Examiner

Marina Miller

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicants' submission filed on 2/06/2006 is acknowledged. Claims 1-13 are pending. Claims 1-13 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

#### ***Claim Rejections - 35 USC § 101***

##### ***Enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of associative analysis for a particular trait, tissue, and/or disease, does not reasonably provide enablement for a method wherein gene expression profiles are classified for false/potential/real positives without reciting specific trait, disease, tissue, and/or a criterium/standard for classifying as positives. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement

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and whether any necessary experimentations is “undue.” These factors include, but are not limited to:

- a) The breadth of the claims;
- b) The nature of the invention;
- c) The state of the prior art;
- d) The level of one of ordinary skill;
- e) The level of predictability in the art;
- f) The amount of direction provided by the inventor;
- g) The existing of working examples; and
- h) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

*In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. 858 F.2d at 740. While all of these factors are considered, sufficient amount for a prima facie case are discussed below.

a) The claims are broad because they are drawn to a generic method for associative analysis comprising identifying a plurality of differentially expressed genes and classifying the differentially expressed genes as false/real/potentially real positives. The instant specification does not provide specific guidance to practice the invention because it does not disclose how to classify differentially expressed genes as false/real positive without knowing a trait, stage of tissue, and/or disease associated with the gene expression. Without knowing for what “trend” genes are classified as positives, the associative analysis would require undue experimentation.

b) The invention is drawn to a method for associative analysis.

c), e) Prior art analysis shows that classifying the differentially expressed genes as positives/negatives requires knowledge of a trait and/or disease. Prior art also supports complex nature of the assessing and classifying the differential gene expression. *See*, for example,

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Dozmorov, *Physiol. Genomics*, 12:239-250 (2003); Troyanskaya, *Bioinformatics*, 18(11):1454-1461 (2002); Xiao, *BMC Genomics*, 3(28) (pages 1-11, Electronic publication) (27 Sep. 2002).

d) The skill of those in the art of molecular biology and bioinformatics is high.

g) The specification provides an example wherein the instant method is used to identify genes that are differentially expressed between normal and dwarf mice. Thus, the specification does not teach a “general” classification of expressed genes as false/real positives without knowing a trait/disease. It does teach how to classify the differentially expressed genes as false/real positives for genes expressed in dwarf mice compared with the expression of genes in normal mice.

h) In order to practice the claimed invention, one skilled in the art must randomly select a trait, disease, disorder, state of tissue, *etc.*, for which the differentially expressed genes are classified as positives. This constitutes undue experimentation.

Due to the undue experimentation required to obtain the goal of the invention in the absence of any recited trait, disease, or disorder, the lack of directions presented in the specification for how to do so, the complex nature of the invention, and the state of the prior art, the specification fails to teach one skilled in the art how to use the claimed method for associative analysis.

### ***Claim Rejections - 35 USC § 112***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

*Answer to Arguments*

The instant claims were previously rejected as being indefinite because it was not clear whether “identifying” and “re-scaling” recited in claim 1 were intended to be active, positive method steps. Applicants argue that the specification on p. 9-10 discusses “identifying” and “re-scaling” as positive steps of the method. In response to the argument, it is noted that the claims do not recite these “limitations” in “active” voice. Therefore, it is still unclear whether the “identification” of outliers and “re-scaling” of the fourth step are merely intended results or are actually active, positive steps of the claimed method. Thus, for the reasons stated above and in the previous office actions, the rejection is maintained.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3-5, 8-9, and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Xiao, BMC Genomics, 3:28 (pages 1-11) (27 Sept. 2002).

Xiao discloses a method of assessment of the differential gene expression comprising steps of collecting gene expression profiles (p. 3-4), normalizing expression profiles in control

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and experimental groups (p. 9), adjusting profiles to identify outliers (p.3, left col.), identifying similarly expressed groups from the control group (p. 3-4, fig. 1), identifying expressed genes by a t-test (p. 3-5, fig. 2-4 and p. 9-10), and classifying expressed genes as false positive using a paired and an associative t-test (p. 4 and 9-10). Thus, Xiao anticipates claims 1 and 8. Xiao discloses selecting genes that are expressed above a background and scaling expression profiles to an average profile of the control group (p. 3), thus anticipating claim 3. Xiao discloses adjusting profiles by applying regression analysis and a deviation from an average profile (p. 3-4, fig. 1), thus anticipating claims 4-5. Xiao discloses an array (p. 1, 2), thus anticipating claim 9. Xiao discloses testing after identifying genes by the associative t-test (p. p. 4, 9), thus anticipating claim 11. Xiao discloses excluding outliers (p. 3), thus anticipating claim 12.

### ***Claim Rejections - 35 USC § 103***

Claims 1-4, 8-9, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dozmorov, *J. Gerontol.*, 57A(3):B99-B108 (March 2002), in view of Alters, US 2002/0072484.

The claims were previously rejected over Dozmorov and Alters. Applicants argue that the Dozmorov publication is not prior art. Applicants also argue that Alters does not disclose classifying gene expression as a likely false positive, real false positive, or potential positive.

In response, it is noted that the Dozmorove publication relied upon in the rejection under 35 U.S.C. 103(a) is different from the Dozmorove publication relied upon in the rejection under 35 U.S.C. 102(a). Dozmorov, *J. Gerontol.*, 57A(3):B99-B108 was published March, 2002, which is earlier than the instant priority date of 10/24/2002, therefore the examiner maintains that Dozmorov is proper prior art.

Applicants are reminded that this is a rejection over a combination of references.

Dozmorov does disclose classifying expressed genes as false positive using a t-test (*e.g.*, false discovery rate, type I and type II error, p. B101, left col. and p. B102, right col.). Alters discloses that following data acquisition, variables are analyzed statistically by paired t-test, Bonferroni method, and t-test comparing the entire population (associative t-test) [0090]. Motivation to combine the references was presented in the previous office action. Applicants do not specifically address the rejection over the combination of references. The examiner maintains that Dozmorov and Alters make the instant claims obvious, and therefore also maintains the instant rejection.

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dozmorov, *J. Gerontol.*, 57A(3):B99-B108 (2002), in view of Alters, US 2002/0072484, as applied to claims 1-4, 8-9, and 12 above, and further in view of Wu, *J. Pathol.*, 195:53-65 (2001).

The claims were previously rejected over Dozmorov, Alters, and Wu. Applicants argue that the Dozmorov publication is not prior art. Applicants also argue that Wu does not disclose classifying gene expression as likely a false positive, real false positive, or potential positive.

In response, it is noted that the Dozmorove publication relied upon in the rejection under 35 U.S.C. 103(a) is different from the Dozmorove publication relied upon in the rejection under 35 U.S.C. 102(a). Dozmorov, *J. Gerontol.*, 57A(3):B99-B108 (2002), relied upon in the instant rejection, is prior art, as set forth above.

Applicants are reminded that this is a rejection over a combination of references.

Dozmorov does disclose classifying expressed genes as false positive using a t-test (*e.g.*, false



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discovery rate, type I and type II error, p. B101, left col. and p. B102, right col.). The examiner maintains that Dozmorov and Alters make obvious the method of claims 1-4, 8-9, and 12, as set forth above. Wu discloses the limitations recited in instant claims 5-7, as set forth in the previous office action. Motivation to combine the references was presented in the previous office action. Applicants do not specifically address the rejection over the combination of references. The examiner maintains that Dozmorov, Alters, and Wu make the instant claims obvious, and therefore also maintains the instant rejection.

### *Conclusion*

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-5, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph. D. can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MM

**MARJORIE A. MORAN**  
**PRIMARY EXAMINER**

*Marjorie A. Moran*  
*4/24/06*

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Examiner  
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